## Remarks

Applicants request reconsideration on the merits of the above-referenced patent application.

### I. Claim amendments

This amendment cancels claim 20 and adds new claim 21. Thus, claims 1-19 and 21 are pending. Claims 1-19 have been amended. Applicants submit that the amendments and new claim 21 do not introduce new matter. Specifically:

Claim 12 has been amended to change the claim dependency so that claim 12 depends from claim 10 rather than claim 11. This amendment corrects an obvious error, as pointed out in the Office action.

Claims 17-19 have been amended to replace "body" with human and/or another animal. New claim 21 likewise is directed to a method for use with a non-human animal. The amendments and new claim 21 are supported by Applicants' specification at, for example, page 11, lines 21-22.

Other amendments rephrase the claims (*e.g.*, make the claim language more consistent), correct grammatical or obvious errors, or remove unnecessary or redundant language. Applicants submit that such amendments are permissible under MPEP §2163.07.

Applicants reserve the right to pursue any canceled subject matter and/or any other subject matter disclosed in this application in one or more divisional and/or continuation applications.

### II. Response to objection to information disclosure statement for being incomplete

The Office action indicates that the July 9, 2004 information disclosure statement did not include a legible copy of each foreign patent reference and non-patent publication. Applicants have enclosed copies of all such references with this Amendment B. Accordingly, Applicants request that the Examiner consider all information provided in the July 9, 2004 information disclosure statement. Because these copies are being submitted after the first substantive Office action in accordance with 37 C.F.R. §1.97(c), the Commissioner is hereby authorized to charge the fee under 37 CFR §1.17(p) to Deposit Account No. **02-2334**.

**III. Response to objection of claim 12 under 37 CFR §1.75(c)**

An objection has been raised to claim 12 for being in an improper dependent form. Applicants request withdrawal of this objection. Claim 12 has been amended to depend from claim 10. Applicants believe the amended dependency is proper, and, therefore, obviates the objection.

**IV. Response to claim rejection under 35 USC §102(b)**

Claims 1-11 and 13 have been rejected under 25 USC §102(b) as being anticipated by Krone (US Patent 5,391,696). Applicants request withdrawal of this rejection.

*A. Claim 1*

Claim 1 is directed to a pharmaceutical composition comprising a polytartrate polymer and at least one pharmaceutically active material. The composition is in the form of a tablet. The tablet is prepared with a press using a compression force of from 10 to 65 $kN/cm^2$. When the tablet is administered to a human or other animal, it is capable of releasing a pharmaceutically active material in a *pulsatile* manner.

In contrast to the composition of claim 1, **Krone fails to disclose any composition releasing an active material in a *pulsatile* manner.** Instead, Krone discusses compositions that reportedly show a *uniform* controlled release of an active substance. *See* Krone, col. 2, lines 21-23. **Krone also fails to disclose any tablet or other composition formed using a compression force of from 10 to 65 $kN/cm^2$.** Thus, for at least these reasons, Applicants respectfully submit that claim 1 is not anticipated by Krone.

*B. Claims 2-11 and 13*

Claims 2-11 and 13 directly or indirectly depend from claim 1, and, therefore, are novel over the cited reference for at least the same reasons as claim 1.

## V. Response to claim rejection under 35 USC §103

Claims 1-20 have been rejected under 25 USC §103 as being obvious over Krone (US Patent 5,391,696) in view of Suzuki (US Patent 6,015,789), and further in view of Remington (Remington's Pharmaceutical Science, Ch. 89, page 1652, 18th edition, 1990) and MacLean (US Publ. Patent Appl. US2002/0094992). Applicants request withdrawal of this rejection.

### *A. Claim 1*

As noted above, Claim 1 is directed to a pharmaceutical composition comprising a polytartrate polymer and at least one pharmaceutically active material. The composition is in the form of a tablet. The tablet is prepared with a press using a compression force of from 10 to 65 $kN/cm^2$. When the tablet is administered to a human or other animal, it is capable of releasing a pharmaceutically active material in a *pulsatile* manner.

*Pulsatile* delivery --- as opposed to *uniform* delivery --- is particularly advantageous for various pharmaceutically active materials, such as vaccines that require a primer dose and a booster dose, actives having a short half-life, actives that are extensively metabolized pre-systematically, and actives (*e.g.*, gonadatropins) that lose their desired therapeutic effect when constant blood levels are maintained. *See, e.g.*, Applicants' specification at page 1, line 11 to page 2, line 6. In accordance with this invention, Applicants discovered that *pulsatile* drug delivery can be attained with a tablet using a polytartrate polymer in a combination with a compression force of from 10 to 65 $kN/cm^2$ when making the tablet. Applicants corroborate this in their Examples on pages 14-17.

In contrast to the composition of claim 1, **Krone fails to teach, suggest, or provide any motivation for a composition releasing an active material in a *pulsatile* manner.** Instead, Krone discusses polytartrate polymer compositions that reportedly show only *uniform* release. *See* Krone, col. 2, lines 21-23. Thus, if anything, a skilled artisan, seeking to develop a *pulsatile* release composition, would have been steered away from polytartrate polymer compositions. This contrary teaching by Krone evidences the nonobviousness of Applicants' composition. *See* MPEP §2145(X)(D)(1) (a prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness).

**Krone also fails to teach or suggest any tablet or other composition formed using a compression force of from 10 to 65 kN/cm$^2$.** Applicants agree with the Examiner's general proposition that some variables in a manufacturing process may be determined through mere optimization without undue experimentation. Applicants, however, respectfully submit that the compression force recited in claim 1 is not a result of mere optimization, but rather an inventive discovery having an unexpected benefit. Specifically, Applicants discovered that this compression force in combination with a polytartrate polymer unexpectedly creates a tablet that is capable of delivering an active ingredient in a *pulsatile* manner. It is believed that the resulting porosity is such that the polytartrate polymer degradation products diffuse through the surface of the tablet at a rate slower than their formation rate. This, in turn, creates a positive pressure inside the tablet that eventually causes the tablet to burst, thereby providing a second pulse of active material. *See, e.g.*, Applicants' specification, page 4, lines 14-19; and page 5, line 32 to page 6, line 7. Krone fails to teach or suggest that a *pulsatile* delivery composition could be achieved with the method recited in claim 1. Instead, Krone discusses compositions for *uniform* delivery, and specifically illustrates the preparation of microparticles using a spray-drying technique and the preparation of rod-shaped implants using an extrusion technique. *See* Krone, Examples 11-12, col. 14, line 57 to col. 15, line 55. This further evidences the fact that the composition of claim 1 would *not* have been obvious to a skilled artisan at the time of Applicants' filing.

The remaining cited references do not cure Krone's deficiencies. Suzuki is simply cited for discussing a tablet containing a GnRH agonist for administration to a human. There is no discussion relating to polytartrate polymer compositions or compositions for *pulsatile* delivery. Although there is discussion relating to controlled release, it is instead focused on *sustained* release. *See, e.g.*, Suzuki, col.. 100, line 8 to col. 102, line 55; col. 168, line 26 to col. col. 170, line 3. Remington, on the other hand, is simply cited for discussing the preparation of multilayer tablets using compression. This discussion is generic, and fails to provide any guidance with respect to polytartrate polymer compositions. Finally, MacLean is simply cited for discussing the administration of an immediate release formulation in combination with a controlled release formulation to increase the overall plasma concentration of an active agent. Although MacLean discusses delayed-release compositions utilizing a bursting core (*see, e.g.*, paragraphs 217 and

270-281), MacLean fails to provide any teaching or suggestion relating to polytartrate polymer compositions capable of *pulsatile* delivery. Thus, none of these additional references teach or suggest the preparation of a polytartrate polymer *pulsatile* delivery tablet, particularly such a tablet prepared using the compression force recited in claim 1.

Simply put, Applicants were the first to discover that a *pulsatile* delivery tablet composition could be prepared using a polytartrate polymer with a compression force of 10 to 65 $kN/cm^2$. The cited art, whether viewed alone or in combination, fails to teach or suggest such a compression force, or any advantages that may stem from it in the context of polytartrate polymer tablet compositions. Thus, the cited art cannot support a *prima facie* showing of obviousness. *See* MPEP §2143 (to support a *prima facie* case of obviousness, the prior art must teach or suggest all the claim limitations). At best, the cited art discusses polytartrate polymer compositions that provide *uniform* release. Thus, if anything, the cited art teaches away from the composition of claim 1 by tying polytartrate polymer compositions to *uniform* --- rather than *pulsatile* --- delivery. For at least these reasons, Applicants respectfully submit that the obviousness rejection of claim 1 must be withdrawn.

*B.* *Claims 2-21*

Claims 2-19 and 21 directly or indirectly depend from claim 1, and, therefore, are patentable over the cited references for at least the same reasons as claim 1.

Claim 20 has been canceled, thus obviating this rejection as to that claim.

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Applicants hereby request a three-month extension to respond to the September 26, 2007 Office action, and authorize the Commissioner to charge Deposit Account No. **02-2334** for the corresponding extension fee. As noted above, the Commissioner also is authorized to charge the fee under 37 CFR §1.17(p) to Deposit Account No. **02-2334** for the submission of the references cited in the July 9, 2004 Information Disclosure Statement under 37 C.F.R. §1.97(c). Applicants do not believe that any other fee is due in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **02-2334**. In addition, if there is ever any other fee deficiency or overpayment under

37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **02-2334.**

Applicants submit that the pending claims are in condition for allowance, and request that this application be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,

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